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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/647,517	01/16/2004	Mylavapu Venkatramesh	16518.132	5271
28381	7590	05/14/2007	EXAMINER	
ARNOLD & PORTER LLP ATTN: IP DOCKETING DEPT. 555 TWELFTH STREET, N.W. WASHINGTON, DC 20004-1206			CARR, DEBORAH D	
		ART UNIT	PAPER NUMBER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/647,517	VENKATRAMESH ET AL.
	Examiner	Art Unit
	Deborah D. Carr	1621

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 20 February 2007.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 71-86 and 89-97 is/are pending in the application.
- 4a) Of the above claim(s) 71-85 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 86 87-97 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>1/04, 10/05</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1621.

Election/Restrictions

2. Applicant's election with traverse of Group II, claims 86, 89-90 and newly added claims 91-97, filed 20 February 2007 is acknowledged. The traversal is on the ground(s) that all the groups could all be searched together as a single entity under one large simultaneous search and would not present any undue search burden. This is not found persuasive because the groups themselves comprise unique DNA sequences encoding functionally distinct enzymes that would each require a distinct search.

Hence, the DNAs and plants comprising them do not constitute a Markush group. Restriction is not based on classification alone, but rather on recognized divergent subject matter, search required, and other factors as articulated in the restriction requirement mailed 12/5/01. Claims should be amended to delete nonelected subject matter.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 71-85 are withdrawn from consideration as being directed to a non-elected invention.

Claim Objections

4. Claims 86, 89-97 is objected to as being drawn to compounds in the context of a product-by-process claim format. The objection is based on the fact that the compounds produced by the process are definite as to their meaning. As such, claims to the compounds can stand-alone. Product-by-process claim language is reserved for situations where the compound cannot be claimed in a definite manner. The instant application does not fall into this category, as the compounds are definite. Further, there is no showing that the process of making imparts new and unobvious properties to the compounds themselves.

Therefore, product-by-process claims 86, 89-97 will be treated as compound claims for the purpose of this examination.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 86, 89-97 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims a recombinant DNA construct comprising a sequence encoding a steroid 5 α -reductase, transformed host cells, methods of making plants transformed with said recombinant construct wherein the seeds of said transformed plants have oil with elevated levels of sitostanol, sitostanol ester, or mixtures thereof; or phytosterol, phytosterol esters, or mixtures thereof when compared to untransformed plants, and the transformed plants thereof.

Applicant describes full-length cDNA encoding steroid 5 α -reductase enzymes, SEQ ID NO: 2 and 4, from *Arabidopsis* and corn respectively, and partial cDNA sequences encoding steroid 5 α -reductase enzymes from soybean, SEQ ID NO: 6 and 8 (page 100, line 30).

Applicant does not describe other DNAs that encode all other steroid 5 α -reductase enzymes from all organisms as broadly claimed. Therefore, it is not clear that Applicant was in possession of the invention as broadly claimed.

See University of California V. Eli Lilly and Co., 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a eDNA encoding that protein from another organism.

The court also addressed the manner by which genus of cDNAs might be described: "A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* At 1406.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 86, 89-97 are rejected under 35 U.S.C. 112, first paragraph, because the specification, is enabling only for claims limited to recombinant constructs comprising *Arabidopsis* and corn cDNAs encoding steroid 5 α -reductase of SEQ ID NO: 2 and 4, as well as transformed host cells, transgenic plants and seeds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant claims a recombinant DNA construct comprising a sequence encoding a steroid 5 α -reductase, transformed host cells, methods of making plants transformed with said recombinant construct wherein the seeds of said transformed plants have oil with elevated levels of sitostanol, sitostanol ester, or mixtures thereof; or phytosterol, phytosterol esters, or

mixtures thereof when compared to untransformed plants, and the transformed plants thereof.

Applicant teaches full length cDNA encoding steroid 5 α -reductase enzymes from Arabidopsis, Soybean, and Corn (Example 2 page 100, line 30), Applicant further teaches prophetically enhancement of sitostanol content in seeds of transgenic plants in transgenic plants engineered to express a 3-hydroxysteroid oxidase and a steroid 5 α -reductase and their analysis by gas chromatography (Example 2 pages 100-101) and enhancement of sitostanol content in seeds of transgenic plants in transgenic plants engineered to express a 3-hydroxysteroid oxidase, a steroid 5 α -reductase and a tocopherol biosynthetic enzyme and their analysis by gas chromatography (Example 7 pages 110).

Applicant does not teach how the DNAs were isolated nor how to isolate other DNAs that encode all other steroid 5 α -reductase enzymes. Also, Applicant does not teach methods of making transformed plants, or seeds thereof, having increased levels of sitosterol, sitostanol ester, or mixtures thereof; or phytosterol, phytosterol esters, or mixtures thereof when compared to untransformed plants.

The metabolic and/or phenotypic effect of expression of transgenes in plants is highly unpredictable. For example, potato transformed with cystathione beta-lyase (CbL) with the intent of increasing the metabolic flux of sulfur metabolism toward the production of methionine, showed over expression of CbL with respect to transcripts and protein but had

no increase of aspartate derived metabolites such as amino acids or pathway intermediates notably methionine (Maimann et al., Enhanced cystathione beta-lyase activity in transgenic potato plants does not force metabolite flow towards methionine, Plants, 2001 Dec., 214 (2), 163-70, see especially Abstract, lines 13-16). Furthermore, an important consideration in genetic engineering for over expression is knowing whether the enzyme is rate limiting and under some kind of regulatory control or influenced by additional mechanisms governing metabolic flux (Broun et al. PNAS July 31,2001 vol. 98 pp8925-8927; see page 8926 second column, 2nd paragraph). Further, the isolation of orthologous DNA sequences from other species introduces an element of unpredictability. The limitation is introduced in finding homologous regions that would adequately enable either PCR amplification or southern hybridization and would entail using either degenerate primers or a probe with limited homology. Thus the screen for orthologous sequences would isolate many genes other than those of interest.

Determining which, if any steroid 5 α -reductase DNA sequences result in overproduction of sterols and tocopherols in transformed plants would require screening a myriad of constructs comprising different DNAs encoding steroid 5 α -reductase and plants transformed therewith. The measurement of relative increases in sterols and tocopherols from seeds in transformants would require trial and error experimentation since no guidance is provided in the specification for screening for the particular phenotype that would arise

from over expression of steroid 5 α -reductase. The isolation of orthologous cDNAs encoding steroid 5 α -reductase would require making and testing of degenerate PCR primers and probes, as well as making and screening a multitude of cDNA libraries with those probes to isolate other cDNAs encoding steroid 5 α -reductase. The testing of the putative positives would entail screening through a host of false positives to isolate other cDNAs encoding steroid 5 α -reductase. Therefore undue experimentation would be required for one of skill in the art.

Given the lack of guidance for isolating DNA sequences encoding steroid 5 α -reductase and producing plants with increased sterol and sterol ester levels in the specification that reflect the breadth of the claims, and the unpredictability in the art, undue trial and error would be needed to practice the invention. Therefore, the invention is not enabled for the scope set forth in the claims.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 86, 89-97 rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claimed inventions encompass untransformed seeds and its oil, which are a product of nature and not one of the five classes of patentable subject matter. Claims 86, 89-90 are drawn to the progeny of the transformed plant. Due to Mendelian inheritance of genes, a single gene introduced into a parent plant would only be transferred at most to half the male gametes and half the female gametes. This translates into only two thirds of the progeny having at least a single copy of the transgene and one quarter of the progeny would not carry a copy of the transgene. Since the claim encompasses progeny that lack the transgene, the claim encompasses plants that are indistinguishable from plants that would occur in nature. See *Diamond v. Chakrabarty*, 447 U.S. 303 (1980), *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 76 USPQ 280 (1948), and *In re Bergy, Coats, and Malik* 195 USPQ 344, (CCPA) 1977. Amendment of the claims to recite that the progeny comprise the construct that was introduced into the parent plant and that the oil is genetically modified would overcome the rejection.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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12. Claims 86, 89-97 rejected under 35 U.S.C. 102(b) as being anticipated by Fernholz et al.

Fernholz et al. teaches an oil containing brassicasterol as one of its components. This oil reads on the instant oil, which only requires that one of the group consisting of brassicastanol, or its ester, stigmastanol, or it ester.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah D. Carr whose telephone number is 571-272-0637. The examiner can normally be reached on Monday-Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or

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access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or
571-272-1000.



DEBORAH D. CARR
PRIMARY EXAMINER

ddc